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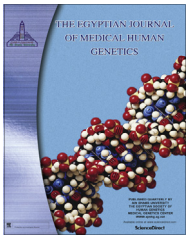

EDITORAL

Subclinical hypothyroidism in children with Down syndrome: To treat or not to treat???

In general, hyperthyrotropinemia and whether to treat or not, is still an unresolved issue. There are no clear guidelines.

Elevated TSH at screening, even when of very short duration, may be a clinically relevant marker of thyroid abnormalities [1]. Data from the Italian National Registry of Infants with Congenital Hypothyroidism reported an association between defects of thyroid development and mild increase of b-TSH at screening. Specifically, 19.6% of babies with a mild increase of b-TSH at screening had defects of thyroid development (thyroid hypoplasia, hemiagenesis, and ectopy) [2].

However, the European Society for Paediatric Endocrinology Consensus Guidelines on Screening, Diagnosis, and Management of Congenital Hypothyroidism, did not reach a solid and clear way of management. They stated that "If venous TSH concentration is $\geqslant$6 to 20 mU/l beyond 21 days in a well baby with a FT4 concentration within the limits for age, we suggest (a) investigation, which should include diagnostic imaging, to try to obtain a definitive diagnosis; (b) consideration, in discussion with the family, of either initiating thyroxine supplementation immediately and retesting, off treatment, at a later stage; or withholding treatment but retesting two weeks later" [3].

In children with subclinical hypothyroidism, The American Thyroid Association in 2014 declared that treatment is generally not recommended when the TSH is 5–10 mIU/L. For patients with a TSH > 10 mIU/L with signs and symptoms consistent with primary thyroid disease and/or risk factors associated with progression, L-T4 replacement may be reasonable. [Weak recommendation Low quality evidence] [4].

As regards Down syndrome (DS), the therapeutic management of subclinical hypothyroidism remains also object of debate. Very few randomized control trials are presented in this field.

The most important question is whether the TSH elevation reflects mild hypothyroidism that could harm brain growth and development in the youngest children with DS and contribute to the ever present mental retardation. An often-used argument against this hypothesis is the finding that accompanying plasma thyroid hormone concentrations generally are within the age-specific normal range. In addition, it is unknown whether thyroid hormone concentrations within the low-normal range always guarantee optimal thyroid hormone provision of the developing brain [5].

A wait and see policy with frequent thyroid function screening could be considered adequate and may be the preferred strategy, thus avoiding chronic hormonal therapy at least in Down syndrome patients in whom TSH levels tend to spontaneously normalize. A positive anti-TPO antibody test is a key factor in the follow-up of these patients because of its potential risk of progression to manifest thyroid disease [6].

Iughetti et al. (2014), suggest that antithyroid antibodies might represent a marker of deteriorating thyroid function unlike 1st year TSH levels that do not predict future thyroid dysfunction requiring therapy, in subjects with DS [7].

Refetoff (2014) would treat hyperthyrotropinemia in DS only if there is evidence for superimposed autoimmunity [8].

In the last paragraph of the editorial, Elsayed mentioned that "L-thyroxine administration will improve growth, hypotonia and psychomotor functions." I would rather use the word "may" instead of "will" improve.

Recently, Bongers-Schokking et al. (2013) reported that congenital hypothyroidism overtreatment during the first 2 years leads to lowered cognitive outcomes at 11 years, whereas undertreatment, if not complicated by overtreatment, results in a normal cognitive development [9].

In conclusion, more evidence is required regarding the optimal course of treatment for subclinical hypothyroidism in DS. Such evidence may be best obtained by conducting a prospective randomized control trial.

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Mohamed El Kholy
Pediatric Hospital, Ain Shams University, Cairo, Egypt
E-mail address: elkholym@link.net

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